Electrophysiological characterization of the human beta cell line EndoC-βH2

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Background and aims: We have characterised the novel human beta cell- line EndoC-βH2 in terms of glucose-induced insulin secretion (GISS), depolarization-evoked exocytosis and properties of voltage-gated ion channels.

Materials and methods: Insulin secretion was tested by static incubations. Secretion rates have been normalised to insulin content. Cytosolic calcium levels ($[Ca^{2+}]_i$) were monitored in cells transfected with the genetically encoded calcium sensor GCaMP5. Exocytosis was assessed by whole-cell capacitance measurement. Membrane potential and currents were recorded using the perforated patch or standard whole-cell technique of the patch-clamp technique. Membrane currents were isolated using specific blockers.

Results: Basal insulin secretion at 1 mmol/l glucose amounted to 2%. Glucose (6 or 20 mmol/l) stimulated insulin secretion 1.5- ($p<0.05$) to 2-fold ($p<0.01$), respectively. This was associated with initiation of action potential firing and elevation of $[Ca^{2+}]_i$. The effects of glucose on insulin secretion, electrical activity and $[Ca^{2+}]_i$ were mimicked by tolbutamide (0.5mmol/l) and reversed by diazoxide (0.2mmol/l), consistent with a key role of ATP-regulated potassium channels. Forskolin potentiated GISS evoked by 6 mmol/l glucose ~3-fold. Exocytosis, evoked by a train of ten 500ms depolarizations, was biphasic with the largest responses occurring during the initial 3 depolarizations with subsequent depolarizations eliciting progressively smaller responses. The cumulative increase of capacitance is of $15 fF.pF^{-1}$ (increase in cell capacitance normalized to cell size, n=9). The contribution of different voltage-gated calcium channels to calcium entry was evaluated using an action potential-like voltage-clamp command (based on spontaneous glucose-induced action potentials recorded in EndoC-βH2 cells). The inward current evoked by the action potential waveform amounted to $8 pA.pF^{-1}$ (n=7) of which 10% was due to tetrodotoxin (TTX)-sensitive sodium channels, 10% due to SNX482-sensitive R-type calcium channels

with the remaining 80% attributable to isradipine-sensitive and ω-agaotoxin-sensitive L- and P/Q-type calcium channels.

Conclusion: The complement of voltage-gated ion channels in EndoC-βH2 is very similar to that seen in primary human beta-cells. We conclude that EndoC-βH2 cell line is good glucose-sensitive model of insulin secretion and electrical activity of primary human beta-cells.